

REMARKS

Claims 11, 18, 20 and 21 have been canceled. Claims 26 to 29 are pending. Claim 26 has been amended to recite Caryophylli Flos extract, which was inadvertently omitted when claim 26 was added in the previous response. This term was present in the originally filed claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Rejections under 35 U.S.C. §103

On pages 2-6 of the Office Action, claims 11, 18, and 20-21 were rejected under 35 U.S.C. §103(a). These claims have been canceled. Therefore, Applicants respectfully request that the rejection be withdrawn.

On pages 6-7 of the Office Action, claims 26-28 were rejected under 35 U.S.C. §103(a) as obvious over US Patent No. 6,497,889 (Takekoshi et al.) in view of US Patent No. 6,495,174 (Niazi) and WO 02/072124 A1 (Kim). Applicants respectfully traverse.

As detailed in the claims and the specification, the present invention comprises a method of promoting hair growth by treating a patient with a pharmaceutical composition comprising at least three components: (1) Asiasari radix extract, (2) a 5 α -reductase inhibitor (selected from at least one of Sophorae radix, Coicis semen extracts and Caryophylli Flos extract), and (3) an activator of hair follicle cells (selected from at least one of hinokitiol and nicotinamide).

The Asiasari radix is extracted with a lower alcohol, n-hexane, or a mixture thereof, and present in an amount of 0.01~10% by weight based on the solid content relative to the total weight of the composition. The inhibitor of 5 α -reductase activity is present an amount of 0.001~10% by weight, and the activator of hair follicle cells is present in an amount of 0.001~10% by weight, based on the total weight of the composition.

The causes of alopecia are very complicated and intricate and many combinations of ingredients have been used in an attempt to cure it. However, not one of the cited

references, whether applied alone or in combination, teaches the specific combination of Asiasari radix extract, 5 α -reductase inhibitor, and activator of hair follicle cells exhibits.

In combining references, the Office Action asserts that "there would have been a reasonable expectation of success in making the claimed invention from the combined teachings of the cited references." The Office Action is thus asserting that the references teach combining the claimed components to arrive at the invention. However, this is not the case. The components are not combined by simple substitution and the invention is not merely an improvement provided by applying known methods. For example, as described more fully below:

- Takekoshi does not disclose Sophorae Radix or hinokitiol as promoting hair growth, but rather as disinfectants. There is no teaching or expectation that these components in the claimed amounts would improve hair growth.
- Niazi discloses capsicum tincture in a complex mixture of herbal extracts. However, there is no suggestion of its use as claimed in combination with other extracts or in the claimed amounts.
- Kim (WO 02/072124) describes extracts for protecting brain cells and improving memory. There is no rationale present for use of the described extract in the claimed combination with the present ingredients in the amounts claimed.

Accordingly, the Office Action provides no rationale to combine the claimed ingredients in the claimed amounts. Applicants note that the Patent Office guidelines require that there be at least some rationale for making the combination (see MPEP 2141). Without this rationale, the claims are not prima facie obvious. Therefore, the rejections should be withdrawn.

Evidence present in the application further supports the nonobviousness of the invention. The inventors have found that using the combination of three ingredients as claimed have a synergistic hair growth promoting effects without side effects. These results are unexpected and advantageous over the prior art, demonstrating the lack of predictability and nonobviousness of the invention.

As shown in Table 3 of the subject application, the compositions comprising all three of the Asiasari Radix extract, the Sophorae Radix extract (an inhibitor of 5 α -

reductase activity) and hinokitiol (an activator of hair follicle cells) (Examples 7 and 8) exhibited distinguished hair growth promoting effects than the compositions comprising one or two of these active ingredients (compare the area ratios of 98.9% and 99.8% of Examples 7 and 8, respectively, with those of other Examples). Such result indicates that the combination of induction of the anagen phase by the Asiasari Radix extract, inhibition of 5 α -reductase activity and activation of hair follicle cells exhibit surprising synergic effects on hair growth promotion. Further, Table 1 shows the anagen phase-induction effect of various concentration of Asiasari Radix extract. In Table 1, 10% solution of Asiasari Radix extract alone exhibited 72.4% of area effect. However, the compositions comprising Asiasari Radix extract in combination with the Sophorae Radix extract and hinokitiol, in which the concentration of Asiasari Radix extract is only 0.5%, exhibited 98.9% (Example 7) and 99.8% (Example 8) of area effect, as shown in Table 3. Such results also show the unexpected synergistic effect derived from the combination of all three components including Asiasari Radix extract, inhibitor of 5 α -reductase activity and activator of hair follicle cells. Accordingly, Applicants have already presented evidence that the claimed invention is not obvious.

Takekoshi *et al.* (US 6,497,889 B2) discloses cosmetics comprising (1) hydroxyproline, an N-acylated hydroxyproline derivative or a salt thereof and (2) at least one component selected from the group consisting of water-soluble vitamins, oil-soluble vitamins, high molecular peptides, high molecular polysaccharides, sphingolipids and seaweed extracts. In Takekoshi *et al.*, plant extract such as *Sophora flavescens* Aiton or *Asarum sieboldii* Miq. and hinokitiol are exemplified as components which may be included in the cosmetics. However, hinokitiol is just exemplified as one of disinfectants and there is no mention as an activation effect of hair follicle cells. Likewise, there is no mention of the effect of inhibition of 5 α -reductase activity of *Sophora flavescens* Aiton or induction of the anagen phase of the hair growth cycle of *Asarum sieboldii* Miq. Further, even though it is described that the cosmetic may be used as hair-growing agent, there are no Examples for showing such hair-growing effect in the description of Takekoshi *et al.* That is, Takekoshi *et al.* neither describes nor suggests the characteristic feature of the subject invention (that is, the combination of Asiasari Radix extract with an inhibitor of

5 α -reductase activity and an activator of hair follicle cells) and does not disclose the unexpected effect resulting from the characteristic feature (that is, synergic effects on hair growth promotion). Accordingly, Takekoshi *et al.* neither anticipates nor renders obvious the subject invention.

Page 3 of the Office Action, acknowledges that Takekoshi does not teach capsicum tincture, concentrations, and lower alcohol extract of Asiasari Radix.

Niazi (US 6,495,174 B1) is directed to a composition comprising of alcoholic extracts of herbs Rhizoma zingiberis recens, Rhizoma pinelliae, Flos carthami, Radix rehmanniae, Radix angelicae sinensis, Radix paeoniae rubra, Cacumen biotae, Semen sesami nigrum, Radix polygoni multiflori, Fructus mori combined with Tincture capsicum, Tincture cantharidinate, and Oleum ricini for direct application to scalp for the treatment of all kinds of alopecia in humans. However, Niazi does not teach or suggest any one of an Asiasari Radix extract, an inhibitor of 5 α -reductase activity or an activator of hair follicle cells, as in the present claims, or suggest the use of capsicum with the components of the present claims. No rationale for making this modification and arriving at the present invention is provided.

Kim (WO 02/072124 A1) is directed to a composition containing Asiasari Radix extracts for protecting brain cells and improving memory. In Kim, Asiasari Radix extracts are extracted with a lower alcohol containing between about 1 carbon atom and about 4 carbon atoms (see claim 4). Even though Kim mentions a composition comprising a low alcohol extracts of Asiasari Radix, it is used to induce neuroprotection against AMPA-induced damages in brain cells as well as stimulation of memory, which is irrelevant to promoting hair-growth. That is, Kim neither describes nor suggests using the alcohol extracts in a way that would arrive at the claimed combination, nor provides a rationale for doing so, much less the characteristic feature of the subject invention (that is, **combination** of an Asiasari Radix extract, an inhibitor of 5 α -reductase activity and an activator of hair follicle cells) and the unexpected effect resulting from the characteristic feature (that is, **synergic** effects on hair growth promotion), nor combining them. Accordingly, Kim neither anticipates nor renders obvious the subject invention and a person skilled in the art would not combine Kim with the other references to arrive at the

present invention.

Considering the above, the cited references, alone or in combination, fail to teach or disclose all limitations of the instant claims, and the combinations do not provide a teaching or suggestion that would motivate one skilled in the art to modify the references to provide the claimed invention. The references also do not teach or suggest the unexpected results obtained using the claimed combination. Applicants respectfully request that the rejection be withdrawn.

CONCLUSIONS

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. Accordingly, Applicants request that the Examiner issue a Notice of Allowance for pending claims 26-29 and that the application be passed to issue. Applicants respectfully request that a Notice of Allowance of the pending claims be timely issued in this case.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

The Commissioner is authorized to charge any deficiency in any patent application processing fees pursuant to 37 CFR §1.17, including extension of time fees pursuant to 37 CFR §1.17(a)-(d), associated with this communication and to credit any excess payment to Deposit Account No. 22-0261.

Respectfully submitted,

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